

22. A method of treating symptoms of diabetes in a human comprising:

a) providing

i) a therapeutically effective amount of conjugated linoleic acid; and

ii) a human patient suffering from diabetes; and

b) administering said therapeutically effective amount of conjugated linoleic acid to said human diabetic patient under conditions such that said symptoms of diabetes are treated.

Remarks

Claims 1-22 are pending in the present application. Claims 1-21 remain pending in the present application and claim 22 is new. In this response, no amendment to claims 1-21 have made. Applicants consider the claims allowable in their present form. Support for new claim 22 can be found throughout the original specification and claims and in particular, on page 14, bottom half and in the examples of the present specification. No new matter has been added by way of the presentation of claim 22. The Examiner has withdrawn her objections/rejections of the presently claimed invention with the exception of her rejection of the present application under 35 U.S.C. §103.

The Examiner maintains her rejection that the present claims are unpatentable under 35 U.S.C. §103 as being obvious over a combination of de Boer, et al., U.S. patent no. 5,518,751 ("de Boer"), in view of Satter, et al., U.S. patent no. 5,770,247 ("Satter"). It is the Examiner's position that de Boer teaches that conjugated linoleic acid ("CLA") in milk is useful to treat diabetes. The Examiner points to column 1, lines 35-43 in support of that view. The Examiner recognizes that de Boer does not teach particularly that CLA is useful in a method of treating diabetes, the specific conjugated linoleic acids claimed or the amount of CLA of the present invention. The Examiner cites Satter for teaching a method of adding linoleic acid compounds into animal feed and cow's milk. Satter is also cited for teaching that linoleic acid compounds to be used may include *trans,cis*-9,11-octadecadienoic acid, *cis,cis*-9,11-octadiendioic acid or

trans,cis-10,12-octadecadienoic acid.

From the teachings of the cited art the Examiner maintains her position that it would have been obvious to employ CLA in a method of treating diabetes and that it would have been obvious for one of ordinary skill in the art at the time the invention was made to incorporate about 1 mg to about 10,000mg/kg of body weight of the *trans,cis*-9,11-octadecadienoic acid, *cis,cis*-9,11-octadiendioic acid or *trans,cis*-10,12-octadecadienoic acid into a milk composition product useful in a method of treating diabetes. Applicants respectfully traverse the Examiner's rejection.

It is respectfully submitted that the Examiner has not made out a cogent case for obviousness. Indeed, it is respectfully submitted that the Examiner has seized on a brief, *ambiguous* general statement in the background section of a U.S. patent to de Boer and combined that ambiguous disclosure with the teachings of Satter which are directed to increasing the CLA content of Cow's milk, to argue that the claimed invention is obvious. As will be argued in detail herein, the Examiner's argument is not cogent and represents a rejection based upon an impermissible *hindsight* reconstruction of the teachings of the two references in rendering the present invention obvious.

Based Upon the Filing Date, de Boer Does Not and Could Not Possibly Teach or Suggest the Use of CLA for Treating Diabetes

Contrary to the Examiner's conclusions regarding the teachings of de Boer, de Boer **does not** disclose or suggest the use of CLA for the treatment of diabetes. In contrast, de Boer merely reiterates and summarizes the state of the art at the time of the filing of de Boer (September 8, 1994). The state of the art on or about September 8, 1994 **did not recognize the significance of CLA in the treatment of diabetes**. Contrary to what the Examiner has posited in making the rejection, the art clearly did not teach or suggest the use of CLA as a treatment modality for

← assertion not supported by any evidence.

diabetes. Indeed, prior to the present application, it was not known that CLA, in contrast to γ -linolenic acid (GLA, commonly found in evening primrose oil, for example), could be used to treat diabetes. Whereas the use of GLA was known in the treatment of diabetes, the use of CLA, prior to the present application, was not known in the treatment of diabetes. CLA differs markedly from γ -linolenic acid and linoleic acid. Indeed, γ -linolenic acid, linoleic acid and CLA have different effects on the human body. This is well known.

A summary of the chemical and biochemical/biological distinctions which exist between CLA on the one hand and linoleic acid or γ -linolenic acid are attached hereto. As indicated in the attached sheets, CLA is known to have an effect on inhibiting mammary and colon cancers, whereas linoleic acid and γ -linolenic acid enhance or promote the formation of mammary and colon cancers. In addition, CLA has a marked effect on body fat (adiposity), lowering body adiposity at 0.1-0.5% of diet by weight, whereas linoleic acid and γ -linolenic acid exhibit little effect on body weight even at substantially higher concentrations (>5% -10% of diet by weight). In addition, CLA is the high naturally occurring ligand for peroxisome proliferator activated receptor (PPAR) responsive genes, whereas linoleic acid and γ -linolenic acid are not high affinity ligands for PPARs and have little effect on the expression of PPAR responsive genes. PPAR has been shown to exhibit substantial effects on the control of metabolism, glucose tolerance, insulin sensitivity and skeletal muscle insulin action. It is because of CLA's impact on PPAR and its selective affinity for the receptor site that CLA exhibits such an unexpected effect in the treatment of diabetes.

irrelevant to the basis of

The Examiner has cited no art, separate from the ambiguous disclosure in the background section of deBoer, which even arguably teaches or suggests the use of CLA (as distinguished from linoleic acid or γ -linolenic acid) for the treatment of diabetes. Indeed, the Examiner must contort the ambiguous disclosure of deBoer because the art actually failed to appreciate the present invention. Prior to the present application, CLA was not known as a treatment modality for diabetes, and indeed, the first report in the literature of the significance of CLA in the

how could the teaching be ambiguous?

treatment of diabetes, was Applicants' own paper, *Biochem Biophys Res Commun*, March 27, 244(3) 678-682 (1998). The date of Applicants' paper is some four (4) years after the filing date of de Boer. A copy of the abstract of that paper was previously enclosed.

Prior to the present application, CLA was known for its anti-carcinogenic and anti-atherogenic properties having cardiovascular implications. Also known in the art was that α -linolenic acid and linoleic acid possess properties which make them potentially useful in the treatment of cardiovascular disease (as indicated by de Boer). Thus, the disclosure in de Boer at column 1, lines 35-43, is completely consistent with the conventional understanding at the time of the filing of that reference and refers to the fact that it was known in the art to use linolenic acid in cardiovascular diseases and diabetes. It was, however, not known in the art, before the present invention that CLA, in contrast to γ -linolenic acid or linoleic acid, could be used for the *treatment of diabetes or that it was a particularly effective treatment for diabetes*.

The ambiguous passage in de Boer, which the Examiner relies on for the teaching that CLA may be used to treat diabetes is found in the background of the invention section at column 1, lines 35-43 and is presented below:

"An important reason for enriching milk or milk powders with fats containing a high percentage of unsaturated fatty acids or strongly unsaturated fatty acids is to prevent or reduce cardiovascular diseases, atrophies, rheumatic disorders or diabetes. In particular, such products contain a high percentage of oleic acid, linoleic acid which may or may not be conjugated, α -linolenic acid and unsaturated C₂₀ and C₂₂ fatty acids."

Thus, even deBoer recognized that the CLA was not a critical component to his milk product (which negates any contention that the DeBoer disclosure anticipates the present invention). Given that CLA was not a critical component to his invention, it is respectfully submitted that de Boer did not appreciate the value CLA has as a treatment modality for diabetes. Rather, a fair reading of that ambiguous passage in the BACKGROUND OF THE INVENTION

*anticipation
assertion*

section of de Boer is that de Boer is merely reviewing the conventional understanding at the time of the filing of de Boer which failed to appreciate the particularly effective use CLA could have in treating diabetes.

Thus, it is accurately argued and concluded, that de Boer merely reiterates a broad discussion of the art which did not teach or suggest the use of CLA for the treatment of diabetes, but rather the use of one or more of the disclosed fatty acids to treat the indicated conditions. It is noted that the Examiner has not separately cited any reference which actually teaches or suggests the use of CLA for the treatment of diabetes and instead, relies on “cherry picking” from the broad general statement in de Boer regarding fatty acids in the background of the invention using a hindsight reconstruction based upon the present application to make the rejection. Thus, de Boer does not and could not teach the use of CLA for the treatment of diabetes, because the use of CLA to treat diabetes was first disclosed in the present application. The only way that de Boer can be read to support the Examiner’s rejection is through an impermissible hindsight reconstruction rejection. To refute Applicants’ contention, the Examiner is encouraged to conduct a search to find a reference which actually discloses the use of CLA for the treatment of diabetes. The undersigned attorney has conducted just such a search and could find no reference which supports the Examiner’s rejection. If it is true, as the Examiner argues, that CLA was known in the art for the treatment of diabetes, given the importance of such a discovery, Applicants, their attorney or the Examiner would surely have been able to find a single reference which discloses CLA for the treatment of diabetes. However, none is available. Instead, the Examiner relies on the ambiguous, non-enabling disclosure of de Boer to make the rejection.

It is respectfully submitted that the Examiner’s reliance on the disclosure in de Boer is insufficient to provide a cogent rejection of the present application on the grounds of obviousness. In order to uphold a finding of obviousness, there must be some teaching, suggestion or incentive for doing what the Applicants have done. See, A.C.S. Hospital Sys. Inc. v. Montefiore Hospital, 723 F.2d 1572 (Fed. Cir. 1984). It is not within the framework of 35

U.S.C. §103 to pick and choose from the prior art only so much as will support a holding of obviousness to the exclusion of other parts necessary for a full appreciation of what the prior art teaches or suggests. Hindsight is not the appropriate test. See, In re Wesslau, 353 F.2d 238 (CCPA 1965). “Both the suggestion and expectation of success must be found in the prior art, not in applicants’ disclosure”. In re Dow Chemical Co., 837 F.2d 469 (Fed. Cir. 1988).

It is respectfully submitted that the proper interpretation of de Boer’s teachings must be read in isolation of the disclosure of the present invention, *not using the teachings of the present invention*. As Applicants have indicated, de Boer’s teaching represents an ambiguous disclosure that CLA may have some use to treat any one of four potential disorders. As of 1994, those of ordinary skill recognized the potential therapeutic impact CLA had in the treatment of cardiovascular disease (because of an effect on cholesterol and lipoproteins) and cancer. Prior to the present invention, CLA was not known for any therapeutic effect in diabetes or, for that matter, for atopies (allergies and related ailments) or rheumatic disorders. Linoleic acid (in contrast to CLA, which is a distinguishable chemical entity) was known for its potential benefit in reducing the impact of rheumatic disorders and atopies (because of an impact on immune system and a reduction in immune disorders), as well as cardiovascular disorders and diabetes. It is noted here that linoleic acid and CLA have quite different biochemical effects and follow separate biochemical pathways in the body. Thus, based upon the disclosure of de Boer, one of ordinary skill would have recognized the value that linoleic acid (not CLA) had for use in a therapeutic modality for treating diabetes.

Prior to the present invention, oleic acid was known for its potential benefit in cardiovascular disease (e.g., its effect on blood pressure and cholesterol synthesis) and diabetes. α -Linolenic acid was known, prior to the present invention, for its potential benefit in cardiovascular disease and stroke, but not diabetes (in fact, γ -linolenic acid was known to be potentially beneficial in diabetes patients) or rheumatoid diseases (α -linolenic acid was known not to be active against rheumatoid diseases) or atopies. C₂₀ fatty acids, such as arachidonic acid

and eicosapentenoic acid, and C₂₂ fatty acids such as docosahexenoic acid, were known to be useful in cardiovascular disease treatment, reducing and/or moderating the effects of atopic diseases, rheumatoid diseases and potentially useful in diabetes (although favorable and unfavorable effects such as increased platelet aggregation in diabetes may be seen).

Thus, the disclosure in deBoers is an accurate reflection of the state of the art in 1994, but is not a teaching that CLA is particularly useful to treat diabetes. The Examiner has contorted the ambiguous teachings of deBoer as that reference relates to CLA and has made out a rejection of the instant application by combining the teachings of the reference with those of the present invention. This construction is impermissible.

Thus, while deBoer represents an accurate, although ambiguous teaching of the state of the art as it relates to the potential therapeutic impact of any one or more of the disclosed fatty acids in one or more of cardiovascular diseases, atopies, rheumatic disorders or diabetes, *deBoer cannot be held to teach the use of any one of the disclosed fatty acids to treat on of the diseased conditions or diseases where the art did not recognize the disclosed fatty acid for that treatment*. It is respectfully submitted that because the art did not recognize that CLA was a particularly useful treatment for diabetes prior to the present invention, the art is clearly deficient and does not make out a cogent rejection of the instant application on obviousness grounds.

It is therefore respectfully submitted that the present invention is clearly non-obvious over the ambiguous and deficient disclosure of deBoer.

Satter Does Not Obviate the Deficiencies of de Boer

Turning to the disclosure of Satter, this reference discloses a method of increasing the CLA content of cow's milk. Satter discloses that CLA has exhibited beneficial effects for humans and discloses a number of beneficial effects, *none of which relate to a favorable*

treatment of diabetes. Those effects are recited at column 1, lines 29-35 and include, reducing body fat and enhancing protein levels in humans and preventing weight loss associated with immune stimulation. However, in Satter, there is no disclosure or even an oblique mention of diabetes or the use of CLA to treat diabetes. Satter is actually devoid of any teaching or suggestion which might be construed to enable one of ordinary skill to combine its teachings with those of de Boer in making a cogent rejection of the instant application.

It is respectfully submitted that a combination of de Boer and Satter does not disclose or suggest the present invention and that these references, in combination, only become relevant to the present invention *after one has read the instant application*. Thus, the Examiner's rejection is an example of hindsight reconstruction, a rejection which is impermissible under the law. See MPEP § 706.02(j) and *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is especially true where, as here, the prior art, *in general*, does not disclose or suggest the claimed invention, and the Examiner relies for such teaching, on an ambiguous description of the prior art. As was stated in *In re Vaeck*, "the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art and not based on applicant's disclosure." *In re Vaeck*, at 20 USPQ2d 1438,1442. Without the reliance of any teaching of the use of CLA for the treatment of diabetes in the prior art other than the putative disclosure in de Boer, Applicants' respectfully submit that the Examiner is engaging in hindsight reconstruction of the invention in make the rejection.

In the present application, there is simply no cogent basis upon which to suggest that the prior art taught the use of CLA for the treatment of diabetes. While the disclosure in de Boer is ambiguous, the prior art would be dispositive of the fact that CLA was not known to be used for the treatment of diabetes. The remaining art cited, Satter, is actually *inapposite* to the teaching. Yet, the Examiner, recognizing the deficiencies in the art, does not separately posit a prior art reference which teaches the use of CLA for the treatment of diabetes. *That is because no independent basis exists for the Examiner's rejection.* Applicants respectfully request the

Examiner to cite whatever prior art may be available for the teaching that CLA is a particularly effective treatment for diabetes, independent of the ambiguous disclosure of de Boer.

It is respectfully submitted that the combination of cited references relied upon by the Examiner fails to render the present invention unpatentable. The first reference, de Boer, fails to teach CLA as a treatment modality for diabetes and the art does not recognize CLA for the treatment of diabetes. The second reference, Satter, totally fails to even mention diabetes or its treatment. It is respectfully submitted that the combined teachings of the art do not make out a cogent obviousness rejection. Moreover, because the Examiner appears to have relied on Applicants' own specification to make the rejection, the obviousness rejection is actually impermissible. Applicants respectfully request the Examiner to withdraw the remaining rejections in the present application and allow this application to issue.

For the above reasons, Applicants respectfully assert that the claims set forth in the present amendment are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited.

Applicant has added 1 independent claim. A fee in the amount \$42.00 (small entity) is therefore due for the presentation of this amendment. The fee of \$370.00 for filing the enclosed Request for Continued Prosecution is enclosed as is the \$42.00 for the newly added claim and the \$55.00 for the petition for a one month extension of time. Please credit any overpayment or charge any additional fee due to Deposit Account No. 04-0838.

Respectfully submitted,

COLEMAN SUDOL SAPONE, P.C.

By: 

Henry D. Coleman

Reg. No. 32,359

714 Colorado Avenue

Bridgeport, Connecticut

(203) 366-3560

Dated: June 14, 2002

Express Mail Certificate

"EXPRESS MAIL" mailing label No.: EL 890 538 296 US

Date of Deposit: June 10, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

Name of person mailing paper:


Henry D. Coleman



APPENDIX

RECEIVED
JUN 19 2002
TECH CENTER 1600/2900

The only amendment to the claims of the present application is that new claim 22 is presented (see below). Previously filed claims 1-21 remain pending in the present application in unamended form.

Please add the following claim 22 to pending claims 1-21 of the present application.

22. (New) A method of treating symptoms of diabetes in a human comprising:

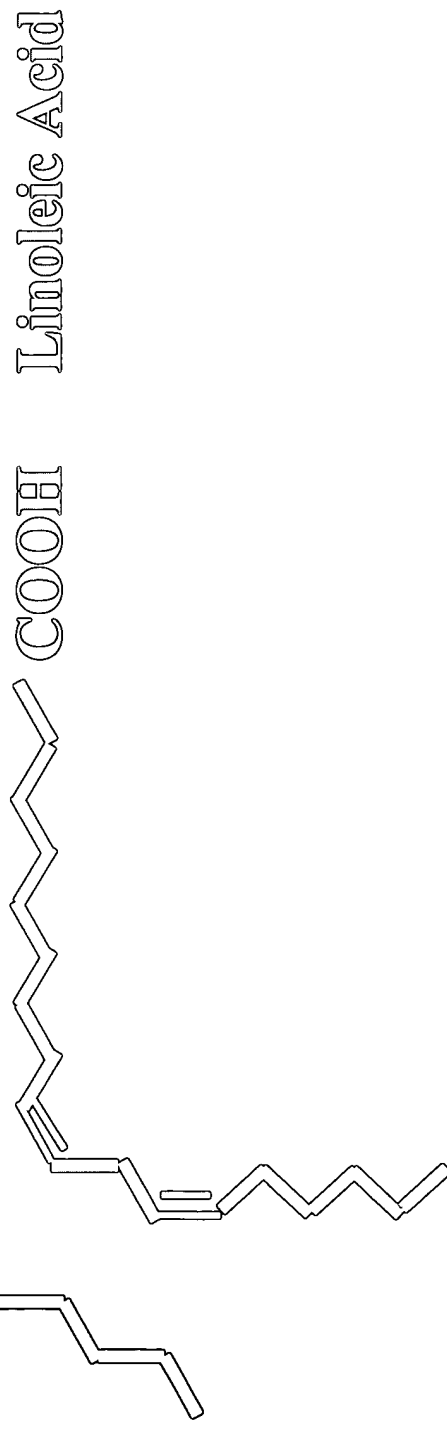
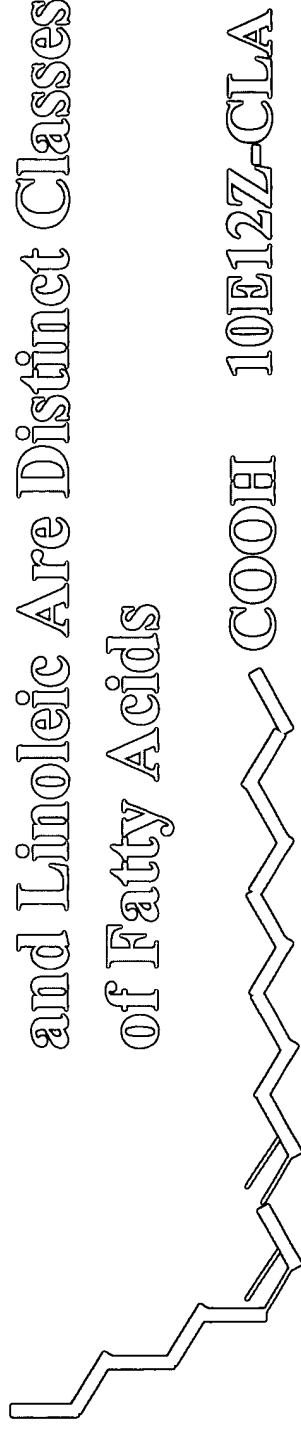
a) providing

i) a therapeutically effective amount of conjugated linoleic acid; and

ii) a human patient suffering from diabetes; and

b) administering said therapeutically effective amount of conjugated linoleic acid to said human diabetic patient under conditions such that said symptoms of diabetes are treated.

Conjugated Linoleic Acid (CLA) and Linoleic Are Distinct Classes of Fatty Acids



CLA vs Linoleic Acid, γ -linolenic acid are Biologically Distinct Fatty Acids

CLA

- Inhibits mammary, colon, cancers
- Is the highest naturally occurring ligand for PPARs
 - Modulates expression of PPAR-responsive genes
- Lowers body adiposity at levels (0.1 – 0.5% of diet by weight)

Linoleic Acid and γ -linolenic acid

- Enhances mammary colon cancers
- Are not a high affinity ligands for PPARs
 - Have little effect on the expression of PPAR responsive genes
- Have little effect on body weight even at higher concentrations ($> 5\%$ - 10% of diet by weight)